Ultrasound Strain and Strain Rate Imaging of Carotid Artery with the Early Sage of Type 2 Diabetes Mellitus

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Abstract- **The objective of this paper is to evaluate the value of ultrasound strain and strain rate imaging in evaluating the motorial characteristics of the early stage of the CCA in patients with type 2 diabetes mellitus (DM2). Fifty patients without vascular complications with type 2 diabetes and fifty healthy volunteers underwent carotid ultrasound are selected as objects in the examinations and the dynamic image was analyzed by the off-line software (syngo Velocity Vector Imaging technology [VVI], Siemens). The results show that Vmax of anterior wall, anterolateral wall and posterolateral wall were higher than those of posterior wall, posteromedial wall, and anteromedial wall ($P<0.05$). VTTP, Vmax, Smax, and SRmax of corresponding segments had significant differences in study group and control group ($P<0.05$). From the results, it could be concluded that Velocity Vector Imaging can be used to evaluate the change of common carotid elasticity in early stage of AS in patients with type 2 diabetes.**

Keywords- Ultrasonography; Velocity Vector Imaging; Speckle Tracking; Common Carotid; Atherosclerosis； Diabetes Mellitus

I. INTRODUCTION

The number of people with diabetes mellitus (DM) in 2010 is estimated to be 285 million, which was approximately 7% of the population of adult in the world [1]. Macrovascular disease, characterized by atherosclerotic changes in large blood vessels, is the major cause of morbidity and mortality (80%) in type 2 DM [1]; cardiovascular disease (stroke) is the leading cause of death in diabetes mellitus patients [2]. The overall relative risk of stroke is 1.5-3 times higher in patients with DM [1]. Recurrent stroke is also twice frequent in patients with DM [3]. More importantly, short- and long-term mortalities after stroke are significantly greater in patients with DM [3]. It has been well established that plaque rupture with subsequent intraluminal thrombosis is the most common cause of acute cardiovascular events [4,5]. Identifying patients at an early stage before clinical complications such as myocardial infarction and stroke occur and assessing the total atherosclerotic burden are clinically important.

Ultrasound is a non-invasive imaging technique, which has been successfully used for the morphological and functional assessment of plaques. It also offers a reliable platform for their biomechanical assessment. Various ultrasound techniques have been used to detect and track the vessel wall motion. Recently, velocity vector imaging (VVI) has been obtained using ultrasounds [6, 7, and 8]

This study aims at exploring the value of velocity vector image(VVI) in evaluating the motorial characteristics of the early stage of Atherosclerotic plague on the CCA in patients with type 2 diabetes mellitus (DM2) and thirty health volunteers underwent ultrasonograph.

II. METHODS

Fifty patients without vascular complications with type 2 diabetes referred to our department for evaluation of cardiovascular status with carotid artery ultrasound were included in the study. Additionally, fifty age and gender matched healthy volunteers without type 2 diabetes mellitus (DM2) in the corresponding period were recruited as controls. General conditions of the patients with type 2 diabetes and the healthy subjects including age, sex, BP, HR,BMI were recorded, and blood sampling indicators such as TG, TC, LDL were examined following over night fasting. All patients gave their informed and written consent to study participation and the human part of the study was approved by the Local Ethics Committee. All patients underwent CCA ultrasound examination. The examined subjects were in supine position, breathe calmly. Neck was fully exposed with face toward opposite side. Ultrasound was performed through transverse and longitudinal directions from up to down according to a standardized protocol over the CCA; images were stored and transferred to a computer for off-line analysis. Intima-media thickness was measured at the point 1cm proximal to the carotid artery bifurcation from the lumen-initial interface to the medial adventitial border [9]. Atherosclerotic plaques were assessed in long axis view of the carotid bifurcation by manual delineation. Presences of plaques were defined as a focal lesion with an IMT of >1.2mm [10]. Two dimensional dynamic image was collected when patient was told to hold breath for several seconds. The dynamic image was stored to be analyzed later. Concisely, the new off-line software (syngo Velocity Vector Imaging technology [VVI], Siemens) provides angle-independent 2D velocity, strain, and SR that was used to derive vessel wall displacement off-line. When the photograph was frozen, twenty-four points were marked on the endomembrane of carotid uniformly by hand. Three sampling points would be added automatically between every two marked points, and the wall of carotid was divided into ninety-six small segments. The reference point was put in the center of lumina. Time to the peak of velocity(VTTP), maximum of velocity(Vmax), maximum of strain(Smax), and maximum of strain rate (SRmax) of six segment (anterolateral wall, anterior wall, anteromedial wall, posteromedial wall, posterior wall, postemlateral wall) were measured, which were supplied by VVI automatic analysis software (Fig. 1). EF and SV were acquired using Simpson's method by 2DE sonograpgy. General average of each index in three continual

heart beating cycles was recorded.

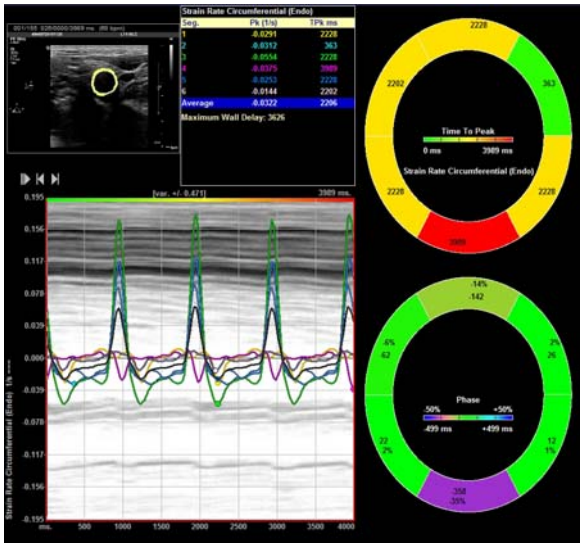

Fig. 1 Example of a velocity vector imaging of the CCA

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Reproducibility of the VVI method is this: for intra-observer variability, the same observer reviewed the ultrasound images and repeated VVI measurements several weeks later during various hemodynamic states. To obtain inter-observer variability, another observer who was blinded to VVI data repeated the VVI measurements.

III. STATISTICAL ANALYSIS

Data are expressed as mean ± standard deviation. Differences in continuous variables between two groups were assessed by unpaired test, and comparison among multiple groups was performed by analysis of variance with ANOVA. Categorical variables were analyzed by Fisher's exact test. Intra- and inter-observer variability was reported as the correlation coefficient between measurements as well as the mean difference between respective measurements. All data analysis was performed by SPSS version 13.0 (SPSS Inc., Chicago, USA). A p value <0.05 was considered Statistical significance.

IV. RESULTS

All patients successfully underwent Carotid artery ultrasound examinations and VVI-measurements could be determined in all investigation. The study group median age was 40.81 years, ranging between 39-51years and the control group median age was 40.17 years, ranging between38-53 years. The relationship between Clinical variables and laboratory analysis in patients and controls are displayed in Table Ⅰ. Age, BP, HR, BMI and SV had no significant differences in the control group and the study group (P>0. 05). IMT of carotid had no significant difference between control group and study group (P>0.05). TG, TC, LDL of the study group were higher than those of control group, HDL in the study group were lower than those in control group, but there were no significant difference between control group and study group (P>0.05). There were significant differences in some segments in control group and study group, where Vmax of anterior wall, anterolateral wall, and posterolateral wall were higher than those of posterior wall, posteromedial wall, and anteromedial wall (P<0.05). VTTP, Vmax, Smax and SRmax of corresponding segments had significant differences in study group and control group (P<0.05). There was no significant difference between any intra- or inter-observer measurements of VTTP, Vmax, Smax, and SRmax.

TABLE Ⅰ RELATIONSHIP BETWEEN CLINICAL AND CCA VARIABLES IN PATIENTS AND CONTROLS

	Study Group	**Control Group**	**P Values**
Clinical Variables			
Age (Yrs)	40.81(39-51)	40.17(38-52)	NS
Body Mass Index (kg/m^2)	21.4(19.45-23.58)	21.7(19.14-24.12)	NS
Blood Pressure (mmhg)			
Systolic	111.4(99-125)	110.9(99-127)	NS
Diastolic	77.5(65-85)	76.8(66-84)	NS
HR(bpm)	71.2(55-81)	70.5(54-80)	NS
Triglycerides (mmol/L)	1.14(0.4–2.9)	1.34(0.5–2.3)	NS
Cholesterol (mmol/L)	5.78(4.2–6.6)	5.65(4.7–8.2)	NS
LDL (mmol/L)	3.89(2.8–5.3)	3.68(3.34–6.4)	NS
HDL (mmol/L)	1.34(1.1–1.8)	1.56(0.8–2.6)	NS
Ef (%)	61.34(55-68)	63.47(56-70)	NS
SV(ml)	74.87(63.59-84.92)	75.81(64.12-86.17)	NS
Bifurcation IMT(mm)	0.95(0.78-1.07)	0.81(0.79-1.02)	NS
VTTP (X10^{2}ms)			
Anterior Wall	1.63(1.41-1.82)	2.21(1.95-2.51)	<0.05

Anterolateral Wall	1.67(1.42-1.90)	2.19(1.96-2.47)	<0.05
Posterolateral Wall	1.63(1.42-1.85)	2.21(1.97-2.55)	<0.05
Posterior Wall	1.71(1.49-1.91)	2.17(1.94-2.45)	<0.05
Posteromedial Wall	1.65(1.43-1.87)	2.12(1.96-2.41)	<0.05
Anteromedial Wall	1.69(1.51-1.92)	2.16(1.93-2.47)	<0.05
Vmax			
Anterior Wall	8.39(6.58-9.69)*	16.13(13.17-19.24)*	<0.05
Anterolateral Wall	8.14(6.25-9.78)*	15.33(12.35-18.56)*	<0.05
Posterolateral Wall	7.92(5.99-8.97)*	13.45(10.08-16.84)*	<0.05
Posterior Wall	1.31(0.99-1.63)	2.36(2.11-2.67)	<0.05
Posteromedial Wall	1.28(0.98-1.64)	1.98(1.68-2.29)	<0.05
Anteromedial Wall	1.36(1.01-1.75)	2.24(1.98-2.64)	<0.05
Smax			
Anterior Wall	5.44(3.16-7.75)	8.11(5.97-10.28)	<0.05
Anterolateral Wall	6.23(3.74-8.68)	9.17(6.91-11.13)	<0.05
Posterolateral Wall	5.98(3.49-8.47)	8.56(6.24-10.33)	<0.05
Posterior Wall	5.36(3.01-7.18)	7.99(5.97-9.24)	<0.05
Posteromedial Wall	5.47(1.66-7.68)	8.27(5.96-10.57)	<0.05
Anteromedial Wall	5.67(3.56-7.79)	8.47(6.18-10.09)	<0.05
Srmax			
Anterior Wall	0.31(0.13-0.49)	0.50(0.29-0.73)	<0.05
Anterolateral Wall	0.29(0.11-0.47)	0.49(0.28-0.72)	<0.05
Posterolateral Wall	0.33(0.17-0.52)	0.53(0.23-0.71)	<0.05
Posterior Wall	0.29(0.15-0.38)	0.49(0.29-0.68)	<0.05
Posteromedial Wall	0.31(0.14-0.49)	0.48(0.31-0.50)	<0.05
Anteromedial Wall	0.28(0.12-0.45)	0.46(0.24-67)	<0.05

Values are presented as median and range unless otherwise stated. * presented as significant differences in some segments in the same groups. LDL=low density lipoprotein cholesterol; HDL=high density lipoprotein cholesterol; IMT=intima-media thickness; VTTP=Time to the peak of velocity; Vmax=maximum of velocity; Smax=maxlmum of strain; SRmax=maximum of strain rate.

V. DISCUSSION

The vascular tissue receives blood pressure and shear stress caused by blood flow during cardiac cycles. Especially, the effect of blood pressure in the radial direction is important in determining 2D tissue velocity. The displacement caused by blood pressure would be large in the soft material and the displacement would be small in the hard material. Whereas displacement and velocity characterize wall motion, strain and strain rate describe wall deformation. The term "strain", which in everyday language can mean "stretching", is used in echocardiography to describe "deformation" [11]. The concept of strain is complex. For a one dimensional (1D) object, the only possible deformation is lengthening or shortening and the linear strain (amount of deformation) can be defined by the formula:

$$\varepsilon = \frac{L - L_0}{L_0} = \frac{\Delta L}{L_0}$$

where ε is strain, L0=baseline length and L=instantaneous length at the time of measurement.

Strain rate (SR) is the rate by which the deformation occurs (deformation or strain per time unit). The unit of strain rate is s−1 and the local rate of deformation or strain per time unit equals velocity difference per unit length:

$$\dot{\varepsilon} = \frac{\Delta\varepsilon}{\Delta t} = \frac{(\Delta L / L_0)}{\Delta t} = \frac{(\Delta L / \Delta t)}{L_0} = \frac{\Delta V}{L_0}$$

Where ΔV is the velocity gradient in the segment studied, L(t) is the length at the time instance t and L(t0) ≡L0.

During recent years, VVI, a novel echocardiographic imaging technique based on routine two-dimensional grayscale echocardiographic images that is independent of the angle of the transducer have emerged as valuable echocardiographic tools for more comprehensive and reliable assessment of myocardial function[12,13]. In order to improve the tracking results, a new algorithm applies a carefully designed sequence of intermediate passages to follow tissue motion accurately through that combines ultrasound speckle tracking, the tissue-blood border detection, global motion coherence, and the consistency of motion between cardiac cycles, thus providing more information than qualitative data. All these passages are calculated with the aid of Fourier techniques that ensure a higher accuracy using the periodicity of the artery motion [14, 15]. In this way, the displacement information of the tracked points is obtained. The intima border is visually identified by the user and manually outlined.

For feature-tracking technique, the pixel features like grey scale are tracked based on cross-correlation algorithm, which incorporates the image grey-scale normalization process [16]. Using such an algorithm, the level of grey-scale intensity will affect slightly the result of feature-tracking method as long as the ultrasonic imaging parameters are kept unchanged during the cineloop acquisition. Such kind of speckle tracking technique has proven accurate at a minimal temporal resolution of 30 Hz [17], which is far below the frame rate used in the current study. Similarly, the accuracy of VVI measurements has been validated by a sonomicrometry technique and a high reproducibility of VVI measurements has been reported by Pirate et al [14] and confirmed by the present study. The method provides a measure of vascular changes of type 2 diabetes mellitus and early detection of vascular wall dysfunction through a new algorithm, combining tracking of ultrasound speckle, the vascular blood interface, and the vascular shape.

Type 2 DM is a disease with both metabolic and vascular components [18]. To our knowledge this is the largest study to date, in which velocity vector imaging has been used to evaluate the biomechanical elasticity of large artery and the change of common carotid elasticity in early stage of AS in patients with type 2 diabetes. By using this technique, we report the quantified elasticity change of differences between the early stage of atherosclerotic plague on the CCA in patients with type 2 diabetes mellitus (DM2) and health volunteers underwent ultrasonography. Our study show the two-dimensional tissue velocity and strain derived by the VVI technique provide important information on tissue character. Age, BP, HR, BMI and SV had no significant differences in the control group and the study group. Although in the early stage of type 2 diabetes mellitus (DM2), the metabolic disorders in patients predominantly included glucose metabolism abnormalities, and dyslipidemia, TG, TC, LDL in the study group were higher than those in control group. HDL in the study group was lower than those in control group, but there were no significant difference between control group and study group. Although IMT of carotid had no significant difference between control group and study group, not surprisingly, patients in the early stage of type 2 diabetes mellitus (DM2) display greater IMT than the healthy subjects because of their systemic atherosclerotic disease. Considering arterial biomechanics, wall shear stress and the circumferential stress acting on the arterial wall traditionally account for vessel wall remodeling during pathological circumstances. There were significant differences in some segments in control group and study group, Vmax of anterior wall, anterolateral wall and posterolateral wall were higher than those of posterior wall, posteromedial wall and anteromedial wall. VTTP, Vmax, Smax and SRmax of corresponding segments of patients in the early stage of type 2 diabetes mellitus(DM2) displayed significantly lower compared to healthy control group. Similarly, the elasticity change of common carotid artery of diabetogenous nephropathy has been reported by Haifei Zheng et al [19]. The comparison demonstrated potential biological significance of this measure in this very initial study. So patients with DM should always control their risk factors and recognize the signs and symptoms of potentially fatal complications as early as possible.

Several limitations of this study should be noted. First, two-dimensional speckle tracking algorithms are inherently dependent on image quality and endocardial border definition. Any technical factors affecting gray scale may in theory have an impact on the accuracy of VVI measurements, so VVI may be considered semi quantitative at present. To reduce these errors to minimum, ultrasonic imaging parameters, such as gain, depth, focus zone, time gain compensation, etc were adjusted to the optimal levels initially and kept unchanged during the entire study. Second, this is only a 2-D ultrasonic imaging model, so the blood flow and the pressure drop were not considered. Third, the residual stress in the atherosclerotic vessels was not considered because present imaging techniques do not allow its quantification. However, VVI is a unique technique for measuring Time to the peak of velocity(VTTP), maximum of velocity(Vmax), maximum of strain(Smax), and maximum of strain rate(SRmax)of the carotid arteries. Further incorporation of VVI in patients with type 2 diabetes may greatly enhance the capability of clinical intervention treatment in earlier period.

VI. CONCLUSION

Vector Imaging can be used to evaluate the change of common carotid elasticity in early stage of AS in patients with type 2 diabetes. Although it is a relatively bigger scale study compared to the previous studies, it is clear that large scale longitudinal studies are necessary to determine the true diagnostic accuracy of these biomechanical characteristics for prediction of clinical risk of future cerebrovascular ischemic events.

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